



Hypothyroidism in Elderly – Review

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Abstract

Hypothyroidism belongs to the group of the most common chronic diseases occurring in the elderly. This is a set of symptoms resulting from elevated serum TSH levels accompanied by a decrease in free thyroid hormone levels, while subclinical hypothyroidism is characterized by an increase in TSH levels at normal fT3 and fT4 levels. This disease is more common in women and the elderly. The basis of the diagnostics of hypothyroidism is testing the serum TSH level at a constant time of day. The aim of the study was to show the most important information about hypothyroidism in the elderly. Awareness in society can increase the chance of detecting this disease and will allow to quickly make a decision about therapy. It has been proven that with age there is a spontaneous increase in TSH concentration, therefore it is important to correctly diagnose older patients in whom the symptoms of the disease may remain unnoticed or justified by the presence of other diseases. In a significant percentage of patients, the disease is iatrogenic caused by adverse drug reactions or thyroid surgery. Untreated disease can result in complications in the form of slowing metabolism, cardiovascular disorders, depression and even hypometabolic coma. Levothyroxine is the drug of choice, a well-balanced diet is also helpful. Therapy should be started with small doses of the drug, closely monitored and selected so that the benefits of treatment outweigh the side effects.

Key words: thyroid gland, hypothyroidism, aged.

Definition and epidemiology

Hypothyroidism is one of the most common chronic diseases occurring in the elderly. We can define it as a set of clinical symptoms caused by the lack or deficiency of thyroxine and/or triiodothyronine, which leads to a slowdown in metabolic processes [1]. Primary hypothyroidism is caused by abnormality in thyroid gland [2]. The second form of hypothyroidism is the central one, which is caused by abnormal function of pituitary gland, hypothalamus or both [3].

Subclinical (latent) hypothyroidism (SHT) is defined as an increase in serum TSH concentration above the upper limit of normal, with normal levels of free thyroxine (FT4) and triiodothyronine [1,4]. Subclinical hypothyroidism gives scanty symptoms and is considered the mildest of all types of hypothyroidism, but in 2–5% cases may progress to overt [5]. Overt hypothyroidism is characterized by the fact that TSH concentration is above the reference range and FT4 levels below the reference range of the population [1].

Most cases of primary hypothyroidism are caused by iodine deficiency and autoimmune diseases, which include Hashimoto. Iodine is a component of thyroid hormones, but is unevenly distributed throughout the world. In Europe, 44% of children consume iodine in insufficient quantities. In countries with normal iodine content, hypothyroidism is 1-2% and increases to 7% in people aged 85–89 [6,7]. Hypothyroidism is about 10 times less common in men than in women [8]. According to the latest research by Mateuszek et al., hypothyroidism is most often diagnosed in postmenopausal women [9].

Pathomechanism

Studies show that aging causes an increase of TSH. The reason for this phenomenon is increased TSH biosynthesis and slowed metabolism. The slowed down distribution of TSH is caused by an increase in the degree of glycosylation of TSH and progressive kidney and liver dysfunction. Ano-

ther change in the aging process is the reduction in total and free triiodothyronine levels despite small changes in thyroxine and free thyroxine levels. Small changes in fT4 concentration are caused by balancing the inhibition of hormone synthesis by its reduced degradation. The reduction of T3 concentration is also caused by a decrease in T3 and T4 production in the thyroid gland. The described disorder of feedback between the hypothalamus, pituitary and thyroid may occur together with a decrease in the sensitivity of peripheral tissues to thyroid hormones. Approximately 30% of women and 10% of older men have positive thyroid peroxidase antibodies, and older people with elevated TSH levels occur in 40-70% of cases. Despite this, only a small group of people who have been shown to have these antibodies develop hypothyroidism [1,10].

An important fact is the high proportion of iatrogenic conditions. The reason may be radioiodine treatment, taking too high doses of thyrostatic agents and side effects of some drugs, for example amiodarone, lithium salts or contrast agents [11,12]. The occurrence of subclinical hypothyroidism may be associated with treatment of symptomatic hypothyroidism with too low dose of levothyroxine [1].

The most common type of thyroiditis is Hashimoto's disease. The essence of the disease is the production of antibodies against thyroid peroxidase and thyroglobulin, which causes destruction of thyroid follicular cells. The highest incidence occurs between 45 and 65 years of age. Studies show that women get sick up to 20 times more often than men, which may be associated with estrogen involvement in pathogenesis. Current research by Sforza et al. indicates that patients with overt hypothyroidism show higher mortality [13,14,15].

Clinical presentation

An uncharacteristic clinical picture of developing hypothyroidism in old age may cause misdiagnosis [16,17]. Symptoms of hypothyroidism include fatigue, memory problems, weakness of tendon reflexes, constipation, dry skin, hair loss and paresthesia, intolerance of coldness, and weight

gain [18,19,20]. In older people, the consequence of hypothyroidism may be a slow heart rate, an increase in arterial stiffness, a decrease in stroke volume, increased coagulation and an increased risk of atherosclerosis. In situations of physical exertion, impairment of left ventricular systolic function may occur. Some researchers say that the coexistence of hypercholesterolemia, constipation, congestive heart failure and macrocytic anemia in an elderly person at the same time may indicate hypothyroidism [16,21]. Hypothyroidism is usually mild, however in extreme cases it may lead to hypometabolic coma increasing probability of death [16,22].

Diagnosis

Diagnosis of hypothyroidism should begin with a serum TSH test. If the patient is hospitalized for another reason, TSH test should not be performed during an exacerbation. When interpreting the result, one should also remember about drugs that may affect the result. It is also good practice to perform the test always at the same time of day, preferably in the morning, which is associated with daily variability of the hormone concentration [16,23,24].

To exclude transient increases in TSH, the test should be repeated after 2-3 months, simultaneously performing an fT4 and thyroid peroxidase antibody test. The presence of a positive titer of anti-TPO antibodies increases the risk of transition to overt hypothyroidism. In older patients, total thyroxine and triiodothyronine levels should be avoided and replaced with fT3 and fT4. This recommendation is directed at the fact that the total concentrations are more strongly influenced by the drugs used, for example estrogens and amiodarone increase while carbamazepine and androgens lower the level of total thyroxine [16,18,23,25].

Indications for treatment

According to the recommendations of the Polish Endocrinological Society, the result of TSH > 10 mIU/l supports the introduction of treatment in

patients with subclinical hypothyroidism, because this level increases the risk of overt disease and cardiovascular incidents [26,27,28]. In patients with asymptomatic disease at $TSH < 10$ mIU/L, without cardiovascular risk factors or thyroid pathology, no indications for treatment have been demonstrated, and in patients with risk factors, treatment should be considered [27]. Especially in patients < 65 years of age with symptomatic hypothyroidism, even if their thyrotropin concentration does not exceed 10 mIU/L [23].

Treatment

Levothyroxine supplementation is used to treat hypothyroidism. In the elderly, it should be introduced starting from small doses: 12.5–25 $\mu\text{g}/\text{day}$, then the amount should be gradually increased by 12.5–25 $\mu\text{g}/\text{day}$ every 4–6 weeks, until the optimal dose. When selecting the dose, it should be taken into account that the need for thyroxine in the elderly is about 20–30% lower [16,29]. Also the patient should be informed that it is not recommended to take levothyroxine with substances that change its absorption, such as fiber, iron and soy milk [30]. The risk of overdose with levothyroxine has been demonstrated in 14–21% of patients. Symptoms of excessive drug supply include nervousness, atrial fibrillation or palpitations [31].

The level of TSH in the elderly during therapy should be 1.0–4.0 mIU/L, and in the younger people 0.5–2.0 mIU/L. After reaching the target value, the serum TSH concentration should be measured again after 2 months, followed by checks every 6–12 months [1,29].

Some patients, especially those with coronary heart disease, may not tolerate the full hormone dose. Cumulative dose once or twice a week should be considered in patients whose condition may interfere with regular hormone intake [29]. According to the latest research by Aziz et al., substitution treatment effectively reduces Carotid Intima-Media Thickness, which is a marker of cardiovascular disease. Before treatment, the pooled weighted mean difference (WMD) of CIMT was 0.44 mm and after treatment a significant decrease to 0.32 mm was achieved [32].

An important aspect of treating hypothyroidism is also a properly selected diet. The iodine content should be 150 µg/day. In the case of Hashimoto's disease, the prophylactic use of a gluten-free diet is not recommended, but only the diagnosis of the patient for celiac disease, which may co-occur with this disease, because according to studies by Collins et al. the dose of LT-4 necessary to maintain euthyrosis in patients with co-occurrence of these diseases decreased after treatment of celiac disease from 154 µg to 111 µg [29,33,34].

Discussion

Studies confirm that one of the causes of hypothyroidism is iodine deficiency or excessive supply and radioactive iodine treatment [35]. The main non-iatrogenic cause of this disease is Hashimoto's disease [36]. Hypothyroidism more often affects women and the elderly [37]. Symptoms associated with hypothyroidism in the elderly are unfortunately often confused with the symptoms of aging [38]. Studies show that changes in the hypothalamic-pituitary-thyroid axis hormone, or TSH, are important in the occurrence of thyroid disease. This is due to changes related with TSH biosynthesis and a slowdown in metabolism [39]. Diagnosis of hypothyroidism should begin with a serum TSH test. The basic substance that is used during treatment is the sodium salt of levorotatory thyroxine [40]. In therapy, in addition to drug therapy, dietary treatment should be introduced, as research confirms that iodine deficiency in the diet may contribute to the impairment of thyroid gland function, therefore an appropriately balanced diet and healthy lifestyle are also important in the treatment of hypothyroidism [36].

Conclusion

Hypothyroidism is a significant problem in the elderly society. Aging affects the functioning of the endocrine organs, including the thyroid gland. The symptoms of hypothyroidism are in many cases difficult to di-

stinguish from the symptoms accompanying old age, so patients should regularly have blood tests and consult disturbing ailments with an endocrinologist. Hypothyroidism, despite the usually mild course, should not be ignored because of the possibility of hypometabolic coma. It can also cause emotional distress, depression or dementia, which significantly reduces the patient's quality of life. The basis for treating hypothyroidism is individually selected pharmacological treatment – mainly levothyroxine supplementation.

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